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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,341	09/16/2003	Alexey Zdanovsky	341.021US1	4133
21186 7590 08/24/2007 SCHWEGMAN, LUNDBERG & WOESSNER, P.A. P.O. BOX 2938 MINNEAPOLIS, MN 55402			EXAMINER PAK, YONG D	
			ART UNIT 1652	PAPER NUMBER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

Application No.

10/664,341

Applicant(s)

ZDANOVSKY ET AL.

Examiner

Yong D. Pak

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 04 June 2007.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-45 is/are pending in the application.
- 4a) Of the above claim(s) 12-14, 21-23, 26-29, 33, 38-40 and 45 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11, 15-20, 24, 25, 30-32, 34-37 and 41-44 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08).  
Paper No(s)/Mail Date \_\_\_\_\_.

- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_.

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on June 4, 2007, has been entered.

Claims 1-45 are pending. Claims 12-14, 21-23, 26-29, 33, 38-40 and 45 are withdrawn. Claims 1-11, 15-20, 24-25, 30-32, 34-37 and 41-44 are under consideration.

### ***Response to Arguments***

Applicant's amendment and arguments filed on April 2, 2007, have been fully considered and are deemed to be persuasive to overcome some of the rejections/objections previously applied.

### ***Claim Objections***

Claim 17 is objected to because the claims drawn to non-elected subject matter, SEQ DI NOs:47, 48, 49, 66, 69-71 and 73-80.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

The rejection of claim 3 and claims 4-7, 15-17, 32-37 and 41-44 depending therefrom under 35 U.S.C. 112, second paragraph, for the recitation of "codons which are preferentially employed in a selected host cell" as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been **withdrawn** in light of the amendment of claim 3.

The rejection of claim 3 and claims 4-7, 15-17, 32-37 and 41-44 depending therefrom under 35 U.S.C. 112, second paragraph, for the recitation of "majority of codons in the open reading frame" as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been **withdrawn** in light of applicant's argument.

Claim 10 and claims 30-31 depending therefrom remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 recites the phrase "nucleic acid sequence encoding at least the reporter protein is optimized". The metes and bounds of the phrase in the context of the above claim are not clear to the Examiner. It is not clear to the Examiner what is considered as "optimized" by the applicants. A perusal of the specification did not provide a clear definition for the above phrase. Without a clear definition, those skilled in the art would

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be unable to conclude if the reporter protein is "optimized for expression in a host cell" without knowing the metes and bounds of the phrase. Examiner requests clarification of the above phrase.

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that the phrase is definite because the specification discloses various sequences for optimizing expression of a nucleic acid sequence. Examiner respectfully disagrees. Page 5 of the specification lists some examples of optimizing nucleic acid sequences in eukaryotes, while the claim instant claim is drawn to optimizing expression of nucleic acids in any host cells. Therefore, the metes and bounds of codons that are "optimized for expression" in any host cell is not clear.

Hence the rejection is maintained.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11, 15-16, 18-20, 24-25, 30-32, 34-37 and 41-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the

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inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-11, 15-16, 18-20, 24-25, 30-32, 34-37 and 41-44 are drawn to a polynucleotide encoding a fusion polypeptide comprising A) a reporter protein or a luciferase and B) at least one or two heterologous protein, such as a PEST sequence or a CL protein of SEQ ID NO:89-98, and/or one or more mRNA destabilization sequence, wherein said fusion polypeptide has a reduced half-life relative to a corresponding reporter protein which lacks the heterologous protein/mRNA destabilization sequences. The claims encompass polynucleotide encoding a fusion polypeptide comprising A) any or all reporter protein or a luciferase and one or more of B) any or all heterologous protein and/or mRNA destabilization sequence, including any or all variants, mutants and recombinants thereof, any or all PEST sequence, including any or all variants, mutants and recombinants thereof and/or CL protein sequences of SEQ ID NO:89-98. Therefore, the claims are drawn to a polynucleotide encoding a fusion polypeptide having any structure. The specification only describes the polynucleotide having the nucleic acid sequence of SEQ ID NO:72, which encodes a fusion polypeptide comprising a specific luciferase isolated from firefly and a specific PEST sequence, a specific CL1. This is not enough and does not constitute a representative number of species to describe polynucleotides encoding a fusion polypeptide comprising a whole genus of variants, recombinant and mutants of any or all reporter protein or luciferase and any or all protein and/or mRNA destabilization sequence or any or all PEST sequences and there is no evidence on the record of the relationship between the

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structure of the polynucleotide of SEQ ID NO:72 and the structure of a polynucleotide encoding a fusion polypeptide comprising any or all recombinant, variant and mutant reporter protein, protein and/or mRNA destabilization sequence or PEST sequences. Therefore, the specification fails to describe a representative species of the genus comprising polynucleotides encoding fusion polypeptides having any structure.

Given this lack of additional representative species as encompassed by the claims, applicants have failed to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at [www.uspto.gov](http://www.uspto.gov).

In response to the previous Office Action, applicants have traversed the above rejection.

Applicants argue that the claims are fully described because the specification exemplifies several luciferases, GFP, protein destabilization sequences and mRNA destabilization sequences and also that said sequences are well known in the art. Examiner respectfully disagrees. The claims are not limited to only those sequences exemplified in the specification and known sequences, but the claims encompass polynucleotide encoding a fusion polypeptide comprising A) any or all reporter protein or a luciferase and one or more of B) any or all heterologous protein and/or mRNA destabilization sequence, including any or all variants, mutants and recombinants

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thereof, any or all PEST sequence, including any or all variants, mutants and recombinants thereof. Therefore, the claims are drawn to a polynucleotide encoding a fusion polypeptide having any structure. In *University of California v. Eli Lilly & Co.*, 43 USPQ2d 1938, the Court of Appeals for the Federal Circuit has held that "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, (or) chemical name,' of the claimed subject matter sufficient to distinguish it from other materials". As indicated in MPEP 2163, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show that Applicant was in possession of the claimed genus. In addition, MPEP 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Applicants argue that the instant specification discloses numerous sequences falling within the scope of the claimed genus, unlike the *UC California v. Eli Lilly* case. Examiner respectfully disagrees. The claims are not limited to only those sequences exemplified in the specification, but the claims encompass polynucleotide encoding a



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fusion polypeptide comprising A) any or all reporter protein or a luciferase and one or more of B) any or all heterologous protein and/or mRNA destabilization sequence, including any or all variants, mutants and recombinants thereof, any or all PEST sequence, including any or all variants, mutants and recombinants thereof. As discussed previously, the recitation of "luciferase", "protein destabilization sequence", "mRNA destabilization sequence" or "PEST sequence" fail to provide a sufficient description of the claimed genus of proteins as it merely describes the functional features of the genus without providing any definition of the structural features of the species within the genus. The CAFC in *UC California v. Eli Lilly*, (43 USPQ2d 1398) stated that: "in claims to genetic material, however a generic statement such as 'vertebrate insulin cDNA' or 'mammalian insulin cDNA,' without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. Similarly with the claimed genus of "luciferase", "protein destabilization sequence", "mRNA destabilization sequence" or "PEST sequence", the functional definition of the genus does not provide any structural information commonly possessed by members of the genus which distinguish the protein species within the genus from other proteins such that one can visualize or recognize the identity of the members of the genus.

Hence the rejection is maintained.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –  
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-7, 10, 20, 25, 35-37 and 41-44 remain rejected under 35 U.S.C. 102(b) as being anticipated by Corish et al.

Claims 1, 4-7, 10, 20, 25, 35-37 and 41-44 are drawn to a polynucleotide encoding a fusion protein comprising a reporter protein and two protein destabilizing sequence and further comprising an inducible promoter and a vector and host cell comprising said polynucleotide, wherein the half life activity of the fusion protein is decreased and said fusion protein has a reduced half-life compared the reporter protein having only one of the destabilizing sequences.

Corish et al. (Protein Eng. 1999 Dec;12(12):1035-40 - form PTO-1449) discloses a polynucleotide encoding a fusion protein comprising a GFP reporter protein and two protein destabilizing sequences, a PEST sequence and a cyclin destruction box, further comprising an inducible promoter, a vector and host cell comprising said polynucleotide, wherein the half life activity of GFP is decreased and said fusion protein has a reduced half-life compared GFP protein having only one of the destabilizing sequences

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(abstract, page 1035 right column, Figure 1 on page 1036 and page 1037). Therefore, the reference of Corish et al. anticipates claims 1, 4-7, 10, 20, 25, 35-37 and 41-44.

In response to the previous Office Action, applicants have traversed the above rejection. Applicants should note that the rejection has been amended.

Applicants argue that the claims are not anticipated by Corish et al. because the presence of both sequences, PEST and a cyclin destruction box (CDB), resulted in a protein having a half-life substantially the same as the protein with only the CDB sequence. Examiner respectfully disagrees. Corish et al. disclose that the GFP alone has a half-life of 26 h (page 1037, 2<sup>nd</sup> paragraph under "Results"), the GFP-PEST fusion protein has a half-life of 9.8 h (page 1037, 2<sup>nd</sup> paragraph under "Results"), the GFP-CDB fusion has a half-life of 5.8 h (page 1037, 4<sup>th</sup> paragraph under "Results") and that the GFP-CDB-PEST fusion protein has a half-life of 5.5 h. Therefore, the fusion protein GFP-CDB-PEST of Corish et al. has a reduced half-life relative to the GFP protein lacking any destabilizing sequences and said fusion protein has a reduced half-life compared GFP protein having only one of the destabilizing sequences (GFP-CDB fusion and GFP-PEST fusion).

Hence the rejection is maintained.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-11, 15-20, 24-25, 30-32, 34-37 and 41-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Leclerc et al., Corish et al., Gilon et al. and Kastelic et al.

Claims 1-11, 15-20, 24-25, 30-32, 34-37 and 41-44 are drawn to (A) a polynucleotide having the nucleic acid sequence of SEQ ID NO:72 which comprises a polynucleotide encoding luciferase isolated from firefly, two protein destabilizing sequence, CL1 sequence of SEQ ID NO:89 (ACKNWFSSLSHFVIHL) and a PEST sequence or (B) a polynucleotide encoding a fusion protein comprising a reporter protein and one or two protein destabilizing sequence or mRNA destabilization sequence and further comprising an inducible promoter and a vector and host cell

comprising said polynucleotide, wherein the half life of expression of luciferase is 20 or 30 minutes.

Leclerc et al. (form PTO-1449) discloses polynucleotide encoding a luciferase isolated from firefly and a PEST sequence obtained from the C-terminal fragment mODC, further comprising an inducible promoter and a vector and host cell comprising said polynucleotide, wherein the half life activity of luciferase is decreased (page 590). The luciferase of the instant invention and the luciferase of Leclerc et al. are identical because both are isolated from the same source, firefly. The PEST sequence of Leclerc et al. is 100% identical to the PEST sequence used by the instant invention (See Figure 1 on page 594 and page 31 of the instant specification). Leclerc et al. discloses that when using luciferase as reporter proteins, owing to the accumulation of residual luciferase (3-4 hour half-life of firefly luciferase), the rapid increase or decreases in gene expression may not be detected (abstract) and that destabilized luciferases having a shorter half-life is advantageous in better quantifying gene expression (pages 590 and 600).

The difference between the reference of Leclerc et al. and the instant invention is that Leclerc et al. does not teach a polynucleotide encoding a fusion protein comprising two protein destabilizing sequences, such as a CL1 sequence, wherein the half life expression of luciferase is 20 or 30 minutes, or a polynucleotide comprising a mRNA destabilizing sequence.

Corish et al. (Protein Eng. 1999 Dec;12(12):1035-40 - form PTO-1449) discloses a polynucleotide encoding a fusion protein comprising a reporter protein and two protein

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destabilizing sequences, a PEST sequence and a cyclin destruction box (page 1035, right column and Figure 1 on page 1036). Corish et al. discloses that the combination of two protein destabilization sequences produced a reporter protein having decreased half life as compared to the reporter protein having one of the protein destabilizing sequences (abstract). Corish et al. discloses that the half-life of luciferase is much shorter than GFP. With this teaching at hand, one having skill in the art would have recognized the advantage to further decrease the half-life of the luciferase of Leclerc et al. by using an additional destabilizing sequences in conjunction with the PEST sequence, such as the cyclin destruction box of Corish et al. or other protein destabilizing sequences known in the art, such as CL proteins, or other methods that decrease expression of proteins, in order to make a reporter protein with a short half life of expression.

Gilon et al. (form PTO-1449) discloses several protein destabilizing sequence, such as a CL1 sequence (ACKNWFSSLSHFVIHL), which is 100% identical to the CL1 sequence of SEQ ID NO:89 (ACKNWFSSLSHFVIHL) (See Table 1 on page 2763 of Gilon et al. and on page 31 of the instant specification).

Kastelic et al. (WO 00/39314 – form PTO-1449) discloses mRNA destabilizing sequences that limit expression of genes of interest (pages 1 and 3) and polynucleotide comprising a reporter DNA and a mRNA destabilizing sequences (page 3). With this teaching at hand, one having skill in the art would have recognized to destabilize luciferase by using one or more protein destabilizing sequences and/or one or more mRNA destabilizing sequences.

Therefore, in combining the teachings of Leclerc et al., Corish et al., Gilon et al. and Kastelic et al., it would have been obvious to one having ordinary skill in the art to make a polynucleotide encoding a fusion protein comprising a firefly luciferase and one or more protein destabilization sequences, such as a PEST sequence and a CL1 sequence, and/or one or more mRNA destabilization sequence. One of ordinary skill in the art would have been motivated to use other protein destabilizing sequences such as the CL sequences of Gilon et al. or a cyclin destruction box sequence as taught by Corish et al. or one or more mRNA destabilization sequences of Kastelic et al. in conjunction with a PEST sequence in order to further reduce the half life activity/expression of luciferase. One of ordinary skill in the art would have had a reasonable expectation of success since Leclerc et al. teaches reducing the half-life activity of a luciferase by using a PEST sequence, Corish et al. teaches that a combination of two protein destabilization sequences protein destabilizing sequences decreases half-life of reporter protein more than using only one of the protein destabilizing sequence, Gilon et al. teaches CL protein destabilizing sequences that can be used to destabilize proteins and Kastelic et al. teaches destabilizing reporter proteins using mRNA destabilizing sequences.

Therefore, the above references render claims 1-11, 15-20, 24-25, 30-32, 34-37 and 41-44 *prima facie* obvious to one of ordinary skill in the art.

In response to the previous Office Action, applicants have traversed the above rejection.

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In response to applicant's arguments against what Corish et al, Gilonet al., and Kastelic et al. does or does not disclose, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants argue that instant claims are not obvious over the cited references because with respect to claim 1, the combination of the cited reference does not disclose or suggest combining protein destabilization sequences so that the resulting fusion protein has a shorter half-life than each of the fusion proteins that have only one of the two protein destabilization sequences. Examiner respectfully disagrees. Corish et al. disclose that the GFP alone has a half-life of 26 h (page 1037, 2<sup>nd</sup> paragraph under "Results"), the GFP-PEST fusion protein has a half-life of 9.8 h (page 1037, 2<sup>nd</sup> paragraph under "Results"), the GFP-CDB fusion has a half-life of 5.8 h (page 1037, 4<sup>th</sup> paragraph under "Results") and that the GFP-CDB-PEST fusion protein has a half-life of 5.5 h. Therefore, the fusion protein GFP-CDB-PEST of Corish et al. has a reduced half-life relative to the GFP protein lacking any destabilizing sequences and said fusion protein has a reduced half-life compared GFP protein having only one of the destabilizing sequences (GFP-CDB fusion and GFP-PEST fusion).

Applicants also argue that with respect to claims 2-3, the combination of the cited references does not disclose or suggest combining a mRNA destabilization sequence and a protein destabilization sequence, or preparing a codon optimized luciferase sequence. Examiner respectfully disagrees. Leclerc et al. discloses that when using



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luciferase as reporter proteins, owing to the accumulation of residual luciferase (3-4 hour half-life of firefly luciferase), the rapid increase or decreases in gene expression may not be detected (abstract) and that destabilized luciferases having a shorter half-life is advantageous in better quantifying gene expression (pages 590 and 600). With this teaching at hand, one having skill in the art would have recognized the advantage to decrease the half-life of the luciferase of Leclerc et al. by using techniques available in the art, by using protein destabilizing sequences or mRNA destabilizing sequences. Since Corish et al. discloses that using two protein destabilizing sequences instead of one further reduces the half-life the GFP protein, one having skilled in the art would have been motivated to also use more than one type of protein or mRNA destabilizing sequences for compounding the effect of destabilizing sequences on the half-life of luciferase. One of ordinary skill in the art would have had a reasonable expectation of success since Leclerc et al. teaches reducing the half-life activity of a luciferase by using a PEST sequence, Corish et al. teaches that a combination of two protein destabilization sequences protein destabilizing sequences decreases half-life of reporter protein more than using only one of the protein destabilizing sequence, Giloni et al. teaches CL protein destabilizing sequences that can be used to destabilize proteins and Kastelic et al. teaches destabilizing reporter proteins using mRNA destabilizing sequences.

Hence the rejection is maintained.

None of the claims are allowable.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Pak whose telephone number is 571-272-0935. The examiner can normally be reached 6:30 A.M. to 5:00 P.M. Monday through Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll free).



Yong D. Pak  
Patent Examiner 1652